

## A P P E N D I X

### Marked-Up Version Showing Changes

#### IN THE SPECIFICATION:

The specification is amended as follows:

Page 10, line 20 to Page 11, line 2, is amended as follows:

"The experiment was conducted in a Huttlin Turbojet Fluid Bed Coater (BWI Huttlin, Daimlerstrasse 7, D-79585, Steinen, Germany) with a 5 L processing container fitted with three bottom spray three-compartment spray nozzle jets and standard 20 micron filter bags. Samples of *Lactobacilli* were sourced from Chr. Hansen of 49 Barry Street, Bayswater, Melbourne, Australia. *Lactobacilli* with *Bafidus* at a ratio of 1:1 was sourced from Gist-Brocade, Australia. These bacteria are anaerobes which easily perish in the presence of oxygen. The trail batch size of the fluidized bed was 4 kg, twice the weight recommended for the 5 L Huttlin Turbojet processing container used, to ensure the fluidized material was close to the processing containers filter giving the best chance for the bacteria to escape through the 20 micron filter. The solid core (tablet granule core materials) comprised 66% w/w dextrose, 13% w/w gelatin, 15% w/w starch. The spraying liquid containing bacteria comprised either  $1.16 \times 10^{12}$  CFU *Lactobacilli*, or  $3.5 \times 10^{12}$  CFU *Lactobacilli/Bifidus*, with 3% w/w mannitol, 1% w/w egg albumin, 1% w/w glycerol, 1% w/w sodium phosphate buffers and made up to 1000 ml with purified water."

Page 35, lines 40-43, are amended as follows:

#### "Enteric Coating Solution

Cellulose Acetate Phthalate [2.00]	0.16kg
Sodium Hydroxide qs to pH 6	
Purified water to 8 kg of total batch size"	

Page 43, lines 7-16, are amended as follows:

"Coating Liquid

Interferon [ $\alpha$ 2] <u><math>\alpha</math> 2b</u> 40 billion IU	
Mannitol	0.200kg
Propylene glycol	0.075kg
Gelatin (succinylated)	0.025kg
Glycine	0.012kg
Egg Albumin	0.001kg
Standard sodium	
phosphate buffers to pH 7	0.073kg
Water for injection to	2.000kg"

Page 43, lines 24-27, are amended as follows:

"1 Inferon  $\alpha$ , glycine, mannitol, gelatin succinylated, propylene glycol, [ascorbic acid] and buffers are dissolved in [purified] water for injection then filtered through 0.22 micron membrane filter. Albumin was added and made up to weight with water for injection."

Page 44, lines 16-24, are amended as follows:

"Coating Liquid

Interferon [ $\alpha$ 2] <u><math>\alpha</math> 2b</u> 40 billion IU	
Mannitol	0.200kg
Propylene glycol	0.150kg
Gelatin (succinylated)	0.050kg
Glycine	0.012kg
Egg Albumin	0.001kg
Standard sodium phosphate buffers to pH 7	0.073kg
[Purified water] <u>Water for injection</u> to	2.000kg"

Page 46, lines 21-31, are amended as follows:

"Coating Liquid

Interferon $\alpha$ 2b 40 billion IU	
Mannitol	0.200kg
Propylene glycol	0.150kg
Gelatin (succinylated)	0.500kg
Glycine	0.120kg
Egg Albumin	0.020kg
Ascorbic Acid	0.057kg
Standard sodium	
phosphate buffers to pH 7	0.073kg
[Purified water] <u>Water for injection</u> to	4.000kg"

Page 50, line 32 to Page 51, line 2, is amended as follows:

"Coating Liquid

Interferon $\alpha$ <u>2b</u> 40 billion IU	
Mannitol	0.200kg
Propylene glycol	0.150kg
Gelatin (succinylated)	0.050kg
Glycine	0.012kg
Egg Albumin	0.001kg
Standard sodium phosphate buffer to pH 7	0.073kg
[Purified water] <u>Water for injection</u> to	2.000kg"

Page 54, Table 12, is amended as follows:

"Table 12

	% w/w
Povidone BP/Eur.P	0.10
Disodium edetate BP/Eur.P	0.14
Polysorbate 80 BP/Eur.P	0.20
Dextran 45,000 BP/Eur.P	0.22
Sodium dihydrogen phosphate BP/Eur.P (Anhydrous Weight)	0.27
Disodium hydrogen phosphate BP/Eur.P (Anhydrous Weight)	0.58
Glycine BP/Eur.P	0.10
Sodium propyl hydroxybenzoate BP/Eur.P	0.03
Sodium methyl hydroxybenzoate BP/Eur.P	0.09
Albumin BPC	0.05
<b>TOTAL</b>	[2.93] 1.78
Purified water BP/Eur.P to	100%"

Page 55, the Table is amended as follows:

"Hydrogel Core	% w/w
Dextrose (anhydrous) BP	46.52
Starch BP (anhydrous wt)	20.00
Gelatin BP/Eur.P (anhydrous wt)	20.00
Carmellose BP (anhydrous wt)	2.00
Coating Liquid	
EPO (Epoetin Alfa) 250,00 IU	
Dextran 40,000 BP/Eur.P	0.600
Sodium Dihydrogen Phosphate BP/Eur.P	0.042
Disodium Hydrogen Phosphate BP/Eur.P (anhydrous wt)	0.057
Glycine BP/Eur.P	0.030
Trehalose	0.600
Sodium Edetate BP	0.025
Propylene Glycol BP	0.050
Egg Albumin [BPC]	5.030
Sodium Chloride BP	0.046
Leucine USP	3.000
TOTAL	[100%] 98%
Purified Water BP/Eur.P to	100%"

Page 55, lines 4-7, are amended as follows:

"1 EPO, dextran, glycine, trehalose, sodium edetate, propylene glycol, sodium chloride, leucine and buffers were dissolved in purified water [for injection] then albumin was added and made up to weight with purified water [for injection]."

Page 58, line 31 to Page 59, line 10, is amended as follows:

"Finally, it is contemplated by the inventors of the present invention that the novel process described herein may be used to prepare other materials and to manipulate materials to particular ends. In particular, it is envisaged that the inventive process may be manipulated to allow for enteric coating of microcapsules using solvents or aqueous methods such as sodium salts of cellulose acetate phthalate, to create sustained release properties by changing the core material polymers to a higher molecular weight or by using a combination of hydrogel core such as high molecular weight gelatin,

polyvinyl pyrrolidone, alginates, carboxymethyl cellulose, various cellulose derivative, polyethylene glycols, albumin, [karregreenin] dextran, carrageenan (one of ordinary skill in the art of formulation will be able to provide various combinations to create a desired release profile), create time release properties by varying the nature of polymers used and the thickness of the coatings and to allow for microdistribution of trace materials among large amount of solid mass."